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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/504,280	02/15/2000	Mike A. Clark	phoe-0057	5368
7590 06/09/2004			EXAMINER	
Woodcock Washburn Kurtz Mackiewicz & Norris LLP One Liberty Place - 46th Floor Philadelphia, PA 19103			ROMEO, DAVID S	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 06/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action**

Application No.

09/504,280

Applicant(s)

CLARK, MIKE A.

Examiner

David S Romeo

Art Unit

1647

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 19 May 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
- ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
- (b) ☐ they raise the issue of new matter (see Note below);
- (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
- (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

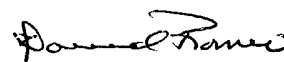
Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 1-8,14-17 and 24.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☒ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). 0405.
10. ☒ Other: See Continuation Sheet

  
David S Romeo  
Primary Examiner  
Art Unit: 1647

Continuation of 5. does NOT place the application in condition for allowance because:

Claims 1-7, 14-17, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsutsumi (AL, cited by Applicants) in view of Satake-Ishikawa (y17) and Ishikawa (n17).

Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsutsumi (AL, cited by Applicants) in view of Satake-Ishikawa (y17) and Ishikawa (n17) as applied to claim 1 above and further in view of Mark (v17).

Applicant argues that the state of the art teaches away from the prior art in the present rejection, and therefore the present claims are not obvious. Applicant's arguments have been fully considered but they are not persuasive. The examiner does not agree with Applicant's characterization of Tsutsumi (Br J Cancer. 1996 Oct; 74(7):1090-5) or that Tsutsumi (Br J Cancer. 1996 Oct; 74(7):1090-5) teaches away from the combination of references in the present rejection because Tsutsumi recognizes PEG molecular weight as a result-effective variable (page 1093; last sentence of paragraph bridging left and right columns; page 1094, right column, last paragraph). Tsutsumi also teaches that when PEG-TNF-alphas were the same molecular size, the TNF-alpha modified with higher molecular weight PEG had a higher bioactivity than when modified with lower molecular weight PEG (page 1091, last sentence of paragraph bridging left and right columns), which provides the motivation to use a higher molecular weight PEG, such as the PEG20,000 taught by Ishikawa. There is no evidence of record that TNF-alpha could not be modified with a higher molecular weight PEG. The only limitation taught by Tsutsumi is with respect to the size of the PEG-TNF-alpha. Tsutsumi does not place any limit on the size of the PEG used to achieve the optimum molecular weight PEG-TNF-alpha.

Claims 1-4, 14-17, 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1-4, 14-17, 24 are indefinite because they recite the term "TNF." Applicant argues that one of skill in the art would be reasonably apprised as to what is meant by the term "TNF." Applicant's arguments have been fully considered but they are not persuasive. The specification intends the term "TNF" to encompass TNF proteins that have been mutated by deletion or alteration of amino acids without significantly impairing biological activity (paragraph bridging pages 5-6). This definition does not clearly set forth the metes and bounds of the claimed invention.

Claims 1, 3, 5-8, 14, 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicant argues that the limitation "15,000" and the limitation "15,000 to about 40,000" are clearly encompassed by the original disclosure. Applicant's arguments have been fully considered but they are not persuasive. With respect to changing numerical range limitations, the written description analysis must take into account which ranges one skilled in the art would consider inherently supported by the discussion in the original disclosure. In the absence of a disclosure of the species "15,000" the specification does not clearly disclose to the skilled artisan that the inventor considered the 15,000 - 40,000 range be part of his invention. Furthermore, a subgenus is not necessarily implicitly described by a genus encompassing it and a species upon which it reads. Just as the description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces, the description of a genus is not necessarily a description of any particular species within the genus..

Continuation of 10. Other: The information disclosure statement (IDS) submitted on 05/06/2004 was filed after the mailing date of the final Office action on 02/03/2004. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner..